

Leukaemia Section

Short Communication

Myeloid/lymphoid neoplasms with eosinophilia and rearrangement of PDGFRA, PDGFRB, or FGFR1, or with PCM1-JAK2: Overview 2019

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Abstract

Review on the group of myeloid/lymphoid neoplasms with eosinophilia and rearrangement of PDGFRA, PDGFRB, or FGFR1, or with PCM1-JAK2 defined by the WHO 2016.

Keywords

eosinophilia; PDGFRA; PDGFRB; FGFR1, PCM1/JAK2

Clinics and pathology

Disease

Eosinophilia is defined as a peripheral blood eosinophil count $> 0.5 \times 10^9/L$, with $> 1.5 \times 10^9/L$ of eosinophil count sometimes referred to as hypereosinophilia. Eosinophilia is a common clinical phenotype associated with various conditions including allergies, infections, medications, autoimmune disorders and malignancies. Although malignancy-related eosinophilia is rare, it is an important clinical sign of these tumors, which require early diagnosis and clinical intervention. Figure 1 summarizes the initial workup of patients with eosinophilia.

Phenotype/cell stem origin

WHO 2016 defines a group of myeloid/lymphoid neoplasms with eosinophilia and rearrangement of PDGFRA, PDGFRB, or FGFR1, or with PCM1 / JAK2 as:

Disease

- (1) Myeloid/lymphoid neoplasms with PDGFRA rearrangement
- (2) Myeloid/lymphoid neoplasms with PDGFRB rearrangement
- (3) Myeloid/lymphoid neoplasms with FGFR1 rearrangement
- (4) Provisional entity: Myeloid/lymphoid neoplasms with PCM1/JAK2

Treatment

This group of patients can be treated with tyrosine kinase inhibitors. While patients with PDGFRA or PDGFRB rearrangement are highly sensitive to Imatinib, PCM1-JAK2 patients had varying responses to JAK2 inhibitor Ruxolitinib, which can induce complete remission, although the duration is often limited. FGFR1 inhibitors have not been very successful in treating tumors with FGFR1 rearrangement. PKC412 was effective in a patient with progressive myeloproliferative disorder with (8;13) (Chen et al., 2004); however, subsequent studies with the FGFR1 inhibitor ponatinib were less successful. Novel FGFR1 inhibitors are currently being tested in clinical trials for solid tumors with FGFR1 activation. Recently a new FGFR family kinase inhibitor INCB054828 induced complete resolution of eosinophilia as well as complete hematologic, cytogenetic and molecular remission in a patient with FGFR1 rearranged MPN (Verstovsek et al., 2018).

Genetics

The fusion partner genes for *PDGFRA*, *PDGFRB*,

or *FGFR1* have been steadily accumulating and are updated below in Tables.

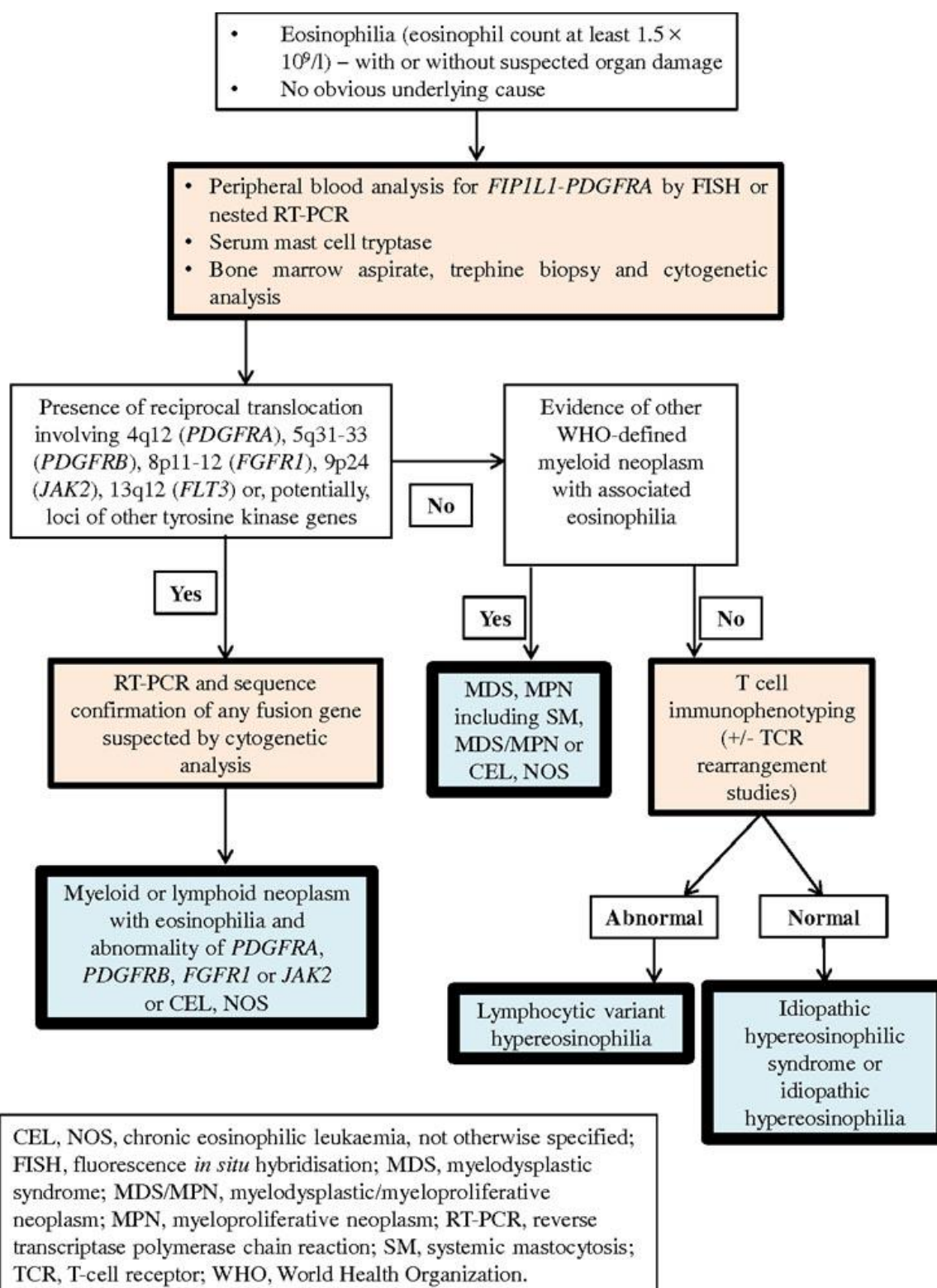


Figure 1. Testing algorithm for possible haematological neoplasms with clonal eosinophilia. Courtesy of the British Committee for Standards in Haematology

Gene name	Rearrangements	Detection methods				Ref (PMID)
		Karyotype	FISH	RT-PCR	NGS	
<i>BCR</i>	t(4;22)(q12;q11.2)	Yes	Yes	Yes	Yes	15034867
<i>CDK5RAP2</i>	ins(9;4)(q33;q12q25)	Yes	Yes	Yes	Yes	16845659
<i>ETV6</i>	t(4;12)(q12;p13)	Yes	Yes	Yes	Yes	17555450
<i>FIP1L1</i>	del(4)(q12q12)	No	Yes	Yes	Yes	12660384
<i>FOXP1</i>	t(3;4)(p13;q12)	Yes	Yes	Yes	Yes	26319757
<i>KIF5B</i>	t(4;10)(q12;p11)	Yes	Yes	Yes	Yes	16498388
<i>STRN</i>	t(2;4)(p24;q12)	Yes	Yes	Yes	Yes	17555450
<i>TNKS2</i>	t(4;10)(q12;q23.3)	Yes	Yes	Yes	Yes	25658984

Table 1: PDGFRA fusion partners, chromosome locations, detection methods and references

Gene name	Rearrangements	Detection methods				Ref (PMID)
		Karyotype	FISH	RT-PCR	NGS	
<i>AGGF1</i>	add(5)	Yes	Yes	Yes	Yes	28552906; 29284681
<i>ATF7IP</i>	t(5;12)(q33;p13)	Yes	Yes	Yes	Yes	24628626
<i>BIN2</i>	t(5;12)(q32;q13)	Yes	Yes	Yes	Yes	20085582
<i>CAPRIN1</i>	t(5;11)(q33;p13)	Yes	Yes	Yes	Yes	17296564
<i>CCDC6</i>	t(5;10)(q33;q21)	Yes	Yes	Yes	Yes	10910073
<i>CCDC88C</i>	t(5;14)(q33;q32)	Yes	Yes	Yes	Yes	15496975; 24772479
<i>CEP85L</i>	t(5;6)(q33-34;q23)	Yes	Yes	Yes	Yes	21938754
<i>CPSF6</i>	t(5;12)(q33;q15)	Yes	Yes	Yes	Yes	26355392
<i>DIAPH1</i>	t(5;5)(q31.3;q32)	No	Yes	Yes	Yes	28751768
<i>DOCK2</i>	del(5)	No	Yes	Yes	Yes	28552906
<i>DTD1</i>	t(5;20)(q33;p11)	Yes	Yes	Yes	Yes	24772479
<i>EBF1</i>	del(5)(q32q33)	No	Yes	Yes	Yes	23835704
<i>ERC1</i>	t(5;12)(q33;p13)	Yes	Yes	Yes	Yes	17690697
<i>ETV6</i>	t(5;12)(q33;p13)	Yes	Yes	Yes	Yes	8168137
<i>GCC2</i>	t(2;5)(q37;q31)	Yes	Yes	Yes	Yes	30697976
<i>GIT2</i>	t(5;12)(q33;q24)	Yes	Yes	Yes	Yes	17296564
<i>GOLGA4</i>	t(3;5)(p22;q31)	Yes	Yes	Yes	Yes	20085582
<i>GOLGB1</i>	t(3;5)(q13;q32)	Yes	Yes	Yes	Yes	26355392
<i>HIP1</i>	t(5;7)(q33;q11)	No	Yes	Yes	Yes	9616134
<i>KANK1</i>	t(5;9)(q32;p24)	Yes	Yes	Yes	Yes	20164854
<i>MPRIIP</i>	t(5;17)(q32;p11)	Yes	Yes	Yes	Yes	26355392
<i>MYO18A</i>	t(5;17)(q32;q11)	Yes	Yes	Yes	Yes	28261327
<i>NDE1</i>	t(5;16)(q32;p13)	Yes	Yes	Yes	Yes	17301821
<i>NIN</i>	t(5;14)(q33;q24)	Yes	Yes	Yes	Yes	15087377
<i>NUMA1</i>	t(5;11)(q32;q13.4)	Yes	Yes	Yes	Yes	28449810
<i>PCM1</i>	ins(8;5)(p23;q33q35)	Yes	Yes	Yes	Yes	29169164
<i>PRKG2</i>	t(4;5)(q21;q33)	Yes	Yes	Yes	Yes	18262053
<i>RABEP1</i>	t(5;17)(q33;p13)	Yes	Yes	Yes	Yes	11588050
<i>SART3</i>	t(5;12)(q32;q23)	Yes	Yes	Yes	Yes	20107158
<i>SATB1</i>	t(3;5)(p24;q32)	Yes	Yes	Yes	Yes	28552906
<i>SPECC1</i>	t(5;17)(q33;p11.2)	Yes	Yes	Yes	Yes	15087372
<i>SPTBN1</i>	t(2;5)(p21;q33)	Yes	Yes	Yes	Yes	18262053
<i>TBL1XR1</i>	(3;5)(q26;q32)	Yes	Yes	Yes	Yes	28509585
<i>TNIP1</i>	t(5;5)(q32;q33)	No	Yes	Yes	Yes	28408464

TP53BP1	t(5;15)(q33;q22)	Yes	Yes	Yes	Yes	15492236
TPM3	t(1;5)(q21;q32)	Yes	Yes	Yes	Yes	16838028
TRIP11	t(5;14)(q33;q32)	Yes	Yes	Yes	Yes	9373237
TSC1	t(5;9)(q32;q34)	Yes	Yes	Yes	Yes	29384404
WDR48	t(1;3;5)(p36;p21;q33)	Yes	Yes	Yes	Yes	20085582
ZMYND8	t(5;20)(q32;q13)	Yes	Yes	Yes	Yes	28408464

Table 2: PDGFRB fusion partners, chromosome locations, detection methods and references

Gene name	Rearrangements	Detection methods				Ref (PMID)
		Karyotype	FISH	RT-PCR	NGS	
BCR	t(8;22)(p11;q11)	Yes	Yes	Yes	Yes	11746971; 11739186
CNTRL	t(8;9)(p12;q33)	Yes	Yes	Yes	Yes	10688839
CPSF6	t(8;12)(p11;q15)	Yes	Yes	Yes	Yes	18205209
CUX1	t(7;8)(q22;p11)	Yes	Yes	Yes	Yes	21330321
FGFR1OP	t(6;8)(q27;p11)	Yes	Yes	Yes	Yes	9949182
FGFR1OP2	t(8;12)(p12;p11); ins(12;8)(p11;p12p22)	Yes	Yes	Yes	Yes	15034873
ERVK-6	t(8;19)(p12;q13)	Yes	Yes	Yes	Yes	12393597

Table 3: FGFR1 fusion partners, chromosome locations, detection methods and references

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